## A FAILED CANCER PARADIGM: Implications for Cancer Risk Assessment and Patients

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The role of the environment in cancer occurrence has been highly disputed over the past 50 years. In the 1970s it was widely believed that environmental factors may account for up to 80% of human cancers. While this was initially thought to relate to the role of environmental contaminants, It became broadened to include diverse lifestyle factors, including diet, medicines and related factors. More recently, the role of environment in human cancer causation has been further questioned within the context of so-called "Bad Luck" mutations, which are claimed to account for some 70% of human cancers, thus greatly diminishing the belief in a dominant role of the environment in cancer causation, especially in the area of chronic low to very low dose exposures which are common in modern industrial societies. In fact, in the US, substantial reductions in exposure to environmental carcinogens in the air, food and drinking water are generally not associated with decreased tumor incidence, with the exception of smoking which should be seen as high dose carcinogen exposure.

A central issue is why cancer incidence and related deaths have not generally declined despite massive national and worldwide efforts to prevent assumed environmentally induced cancers and similar massive efforts to treat such affected individuals with research based therapeutic approaches. The striking failures to prevent the occurrence of cancer and a similar failure to markedly improve survival of cancer patients suggests that something is fundamentally wrong with current accepted paradigms of cancer. This compels the reevaluation of not only our basic understanding of the biology of cancer but also the functional predictive utility of cellular and animal models in both a qualitative and quantitative sense. It is also suggests that the biostatistical models that used by regulatory agencies to estimate risks at low doses and upon which environmental standards are based may also provide highly unreliable information. Yet, environmental health beliefs and regulatory strategies are based on these approaches, typically without evidence of probing reflection by regulatory

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agencies and other leading groups that seem to be locked into dominating paradigms that have yielded profound scientific and clinical failure.

This situation calls for a top to bottom reappraisal of the "cancer problem". This challenge is central to society. Vast resources have been directed to prevent and cure this devastating disease, without the long hoped for successes. Despite the many collective trillions of dollars spent and vast research advances in many areas over a five decade period the results are so strikingly anemic and so far off the mark to indicate that current fundamental understandings are seriously wrong and in need of a drastic rethinking and midcourse corrections.

As an initial step, there needs to be an objective and sober evaluation of the progress or lack thereof at multiple levels: theoretical, experimental, modeling and therapeutic. Many of these research areas do not typically communicate but there is a need for a genuine integrative new synthesis. In the late 1970s under the administrative and scientific leadership of Eula Bingham, OSHA directed a national effort to develop a general scientific consensus to assess cancer risks from low doses of chemical and physical agents. Hundreds of experts testified with the information then synthesized and integrated, resulting in a massive publication in 1980. This effort was used by regulatory agencies to understand the cancer risk assessment issue and to formulate standard setting and create research priorities. Now some 40 years later it is clear than far more needs to be done; society can not continue along the same path and expect a different and improved outcome. A new national leadership effort should be initiated under the aegis of the EPA and the NCI to address how societal efforts can lead to vastly improved understandings of the causation and successful treatment of cancer. The former OSHA approach would be a good one to revisit as there needs to be a formal means by which agencies such as EPA and NIH/NCI can listen to scientific thought leaders in hopes of making the next 40 year period one in which it can deliver on the massive financial investments made to drastically reduce the incidence of cancer and make its clinical treatments far more successful.